



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 15/12, 5/10, 1/21, C07K 14/705, 14/72, 16/28, A61K 38/17, C12Q 1/68		A3	(11) International Publication Number: WO 00/20590
			(43) International Publication Date: 13 April 2000 (13.04.00)
(21) International Application Number: PCT/US99/23317		1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 95006 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AZIMZAI, Yalda [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US). (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 6 October 1999 (06.10.99)			
(30) Priority Data:			
09/167,219 6 October 1998 (06.10.98) US 60/172,211 6 October 1998 (06.10.98) US 60/133,585 11 May 1999 (11.05.99) US			
(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications			
US 09/167,219 (CIP) Filed on 6 October 1998 (06.10.98) US 60/172,211 (CIP) Filed on 6 October 1998 (06.10.98) US 60/133,585 (CIP) Filed on 11 May 1999 (11.05.99)			
(71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US).			
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		Published With international search report. (88) Date of publication of the international search report: 20 July 2000 (20.07.00)	

(54) Title: G-PROTEIN COUPLED RECEPTOR PROTEINS

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(57) Abstract

The invention provides human G-protein coupled receptor proteins (GCRP) and polynucleotides which identify and encode GCRP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GCRP.

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EE	Estonia						

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PF-0612 PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 23317	International filing date (day/month/year) 06/10/1999	(Earliest) Priority Date (day/month/year) 06/10/1998
Applicant INCYTE PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒

contained in the international application in written form.

☒

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority in written form.

☐

furnished subsequently to this Authority in computer readable form.

☐

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒

as suggested by the applicant.

☐

because the applicant failed to suggest a figure.

☐

because this figure better characterizes the invention.

1A

☐

None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/23317

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 17,18,20
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see additional sheet, invention 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 17,18,20

Claims 17, 18 and 20 refer to an agonist, an antagonist and to the use of an antagonist of the polypeptide of claim 1 without giving a true technical characterization. Moreover, no such compound is defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such speculative claims the wording of which is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Invention 1: claims 1-20 all partially
A substantially purified polypeptide comprising an amino acid sequence of SeqIdNo.1, a fragment of said polypeptide, a variant polypeptide having at least 90% sequence identity to said polypeptide; an isolated and purified polynucleotide encoding said polypeptide, a variant polynucleotide having at least 70% sequence identity to said polynucleotide, a polynucleotide hybridising to said polynucleotide, a polynucleotide having a sequence complementary to said polynucleotide; a detection method using said complementary polynucleotide; a polynucleotide comprising a sequence of SeqIdNo.9 or a fragment thereof, a polynucleotide having at least 70% sequence identity to said polynucleotide of SeqIdNo.9, a polynucleotide complementary to said polynucleotide of SeqIdNo.9; expression vector, host and recombinant method related thereto; a pharmaceutical composition comprising said polypeptide of SeqIdNo.1 or fragment of said polypeptide of SeqIdNo.1; an antibody to said polypeptide of SeqIdNo.1 or fragment of said polypeptide of SeqIdNo.1; an agonist to said polypeptide of SeqIdNo.1; an antagonist to said polypeptide of SeqIdNo.1; therapeutic application thereof

2. Inventions 2-7: claims 1-20 all partially
Idem as for subject 1 but limited to each of the polypeptide sequences as in SeqIdNo.3-8 and the corresponding polynucleotide sequences as in SeqIdNo.11-16, wherein respectively invention 2 is limited to SeqIdNo.3 and SeqIdNo.11, invention 3 is limited to SeqIdNo.4 and SeqIdNo.12, ..., invention 7 is limited to SeqIdNo.8 and SeqIdNo.16

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IS 99/23317

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/12 C12N5/10 C12N1/21 C07K14/705 C07K14/72 C07K16/28 A61K38/17 C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K A61K C12Q		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBEST30 [Online] E.M.B.L. Databases Accession Number: C17798, 4 October 1996 (1996-10-04) FUJIWARA T ET AL: "Human placenta cDNA 5'-end GEN-553A03" XP002130338 99.8% identity in 556 bp overlap with SeqIdNo.9 abstract	3-6
P,X	--- WO 99 46281 A (BAKER KEVIN P ;CHEN JIAN (US); GENENTECH INC (US); GURNEY AUSTIN () 16 September 1999 (1999-09-16) Human PRO1083: 100.0% identity in 693 aa overlap with SeqIdNo.1 / 99.9% identity in 3574 bp overlap with SeqIdNo.9 --- -/--	1-16,19
<div style="display: flex; justify-content: space-between;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex. </div>		
<div style="display: flex;"> <div style="flex: 1;"> <p>* Special categories of cited documents :</p> <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="flex: 1;"> <p>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>*&* document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search <div style="text-align: center; font-size: 1.2em;">11 February 2000</div>		Date of mailing of the international search report <div style="text-align: center; font-size: 1.2em;">16. 05. 2000</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer <div style="text-align: center; font-size: 1.2em;">Lonnoy, 0</div>

INTERNATIONAL SEARCH REPORT

International Application No.
US 99/23317

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 15551 A (GARVAN INST MED RES ;HERZOG HERBERT (AU)) 1 April 1999 (1999-04-01) TSR32: 99.9% identity in 693 aa overlap with SeqIdNo.1 / 99.7% identity in 2699 bp overlap with SeqIdNo.9 ---	1-16,19
A	EP 0 805 204 A (INST HORMON UND FORTPFLANZUNGS) 5 November 1997 (1997-11-05) ---	
A	WO 96 18651 A (ELLIS CATHERINE ELIZABETH ;SMITHKLINE BEECHAM CORP (US); BERGSMA D) 20 June 1996 (1996-06-20) ---	
A	STADEL J M ET AL: "Orphan G protein-coupled receptors: a neglected opportunity for pioneer drug discovery" TRENDS IN PHARMACOLOGICAL SCIENCES,GB,ELSEVIER TRENDS JOURNAL, CAMBRIDGE, vol. 18, no. 11, November 1997 (1997-11), page 430-437 XP004096215 ISSN: 0165-6147 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/23317

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because they relate to subject matter not required to be searched by this Authority, namely:
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see FURTHER INFORMATION sheet PCT/ISA/210
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Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
see additional sheet, invention 1.

Remark on Protest

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- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 17,18,20

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2. Inventions 2-7: claims 1-20 all partially

Idem as for subject 1 but limited to each of the polypeptide sequences as in SeqIdNo.3-8 and the corresponding polynucleotide sequences as in SeqIdNo.11-16, wherein respectively invention 2 is limited to SeqIdNo.3 and SeqIdNo.11, invention 3 is limited to SeqIdNo.4 and SeqIdNo.12, ..., invention 7 is limited to SeqIdNo.8 and SeqIdNo.16

INTERNATIONAL SEARCH REPORT

... on patent family members

Initial Application No

/US 99/23317

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9946281 A	16-09-1999	AU 3072199 A	27-09-1999
		AU 3075099 A	11-10-1999
		WO 9947677 A	23-09-1999
		AU 1532499 A	15-06-1999
		WO 9927098 A	03-06-1999
		AU 3757099 A	08-11-1999
		WO 9954467 A	28-10-1999
		AU 1070399 A	10-05-1999
		WO 9920756 A	29-04-1999
WO 9915551 A	01-04-1999	AU 9330098 A	12-04-1999
		EP 0973800 A	26-01-2000
EP 0805204 A	05-11-1997	DE 19617940 A	30-10-1997
WO 9618651 A	20-06-1996	AU 4522796 A	03-07-1996
		EP 0871669 A	21-10-1998
		JP 10511936 T	17-11-1998
		ZA 9510686 A	03-07-1996